510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE

A. 510(k) Number:
K041148

B. Purpose for Submission:
Device clearance. Use of a spectrophotometer in conjunction with C-urea breath tests for the detection of Helicobacter pylori infection

C. Analyte:
$^{13}CO_2$ content of breath CO_2 gas due to the presence of H. pylori.

D. Type of Test:
Quantitative infrared spectroscopic analysis

E. Applicant:
Otsuka Pharmaceutical Co., Ltd

F. Proprietary and Established Names:
POCone Infrared Spectrophotometer

G. Regulatory Information:

1. Regulation section:
   21 CFR Part 862.2300, colorimeter, photometer or spectrophotometer for clinical use
   21 CFR Part 866.3110, Campylobacter fetus serological reagents
2. Classification:
   Class 1
   Class 1
3. Product Code:
   JJQ – Colorimeter, photometer or spectrophotometer for clinical use
   MSQ – Urea breath tests
4. Panel:
   75 – Clinical Chemistry and Clinical Toxicology
   83 - Microbiology

H. Intended Use:

1. Intended use(s):
   The POCone Infrared Spectrophotometer is an in vitro diagnostic device designed to measure changes in $^{13}CO_2$ content in breath CO_2 gas by infrared spectroscopic analysis. The POCone Infrared Spectrophotometer is intended for use in conjunction with commercially available Meretek ^{13}C-urea breath tests for the detection of Helicobacter pylori infection, and Otsuka Breath

Collection Bags. The POCone is suitable for use in both clinical laboratory and point-of-care settings.

2. Indication(s) for use:
   The POCone Infrared Spectrophotometer is an in vitro diagnostic device designed to measure changes in $^{13}CO_2$ content in breath CO_2 gas by infrared spectroscopic analysis. The POCone Infrared Spectrophotometer is intended for use in conjunction with commercially available Meretek ^{13}C-urea breath tests for the detection of Helicobacter pylori infection. The POCone Infrared Spectrophotometer is suitable for use in both point-of-care and clinical laboratory settings.

3. Special condition for use statement(s):
   The POCone spectrophotometer is for prescription and point-of-care use

4. Special instrument Requirements:
   N/A

I. Device Description:

The POCone Infrared Spectrophotometer is a compact, easy to operate analyzer designed for on-site performance of the ^{13}C-urea breath test. For the test the patient provides an initial breath sample (reference or baseline) by blowing into an Otsuka breath collection bag. After ingestion of ^{13}C-labeled urea and after a specified period of time, another breath sample is provided (test or post dose) by blowing into a second breath collection bag. The bag includes a mouthpiece and port compatible with the inlet ports of the POCone. The mouthpiece end of the bag has a one way valve which prevents loss of breath sample. The POCone has 2 ports for attaching the breath collection bags. After attachment, the reference and test breath samples are automatically injected and measurements are performed by the POCone for approximately 2 minutes. User interface with the POCone is by means of a keypad and LCD screen on the front panel. An internal printer is provided to allow subject information and test results to be printed. Software embedded in the instrument controls several functions of the device operation.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   UBiT-IR 300 Infrared Spectrometry System
2. Predicate K number(s):
   K013371
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	Measures changes in $^{13}CO_2$ content in breath for detection of H. pylori	Measures changes in $^{13}CO_2$ content in breath for detection of H. pylori

	infection	infection.
Test sample	Breath sample collected in specially designed breath collection bags	Breath sample collected in specially designed breath collection bags
Detection method	Infrared spectrophotometer	Infrared spectrophotometer
Cut-off value (using Meretek UBT breath test)	2.4 Delta over baseline	2.4 Delta over baseline
User setting	Point of Care or Clinical Laboratory	Point of Care or Clinical Laboratory
Application	For use with Meretek UBT Breath test for H. pylori	For use with Meretek UBT Breath test for H. pylori

Differences		
Item	**Device**	**Predicate**
System components	POCone Infrared Spectrophotometer (with built-in computer) Breath collection bag	IBiT-IR 300 Infrared Spectrophotometer (with built in computer) UBiT – AS10 Autosampler Breath collection bag
Main unit dimensions	220mm width by 361 mm depth by 272 mm height. Weight 10 kg.	310mm width by 620 mm depth by 310 mm height. Weight 22.5 kg
Time frames	Measuring time 2 minutes Warm up time 10 minutes (max. 30 minutes)	Measuring time 5 – 6 minutes Warm up time 40 minutes (max. 80 minutes)

K. Standard/Guidance Document Referenced (if applicable):

- Review criteria for assessment of laboratory tests for the detection of antibodies to Helicobacter pylori.
- Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline EP5-A NCCLS
- FDA Guidance for the content of premarket submissions for software contained in medical devices

L. Test Principle:

The principle of measurement of the POCone spectrophotometer is based on the utilization of the difference between the specific absorptions of $^{13}CO_2$ and $^{12}CO_2$ in the infrared region. When breath samples collected in breath collection bags are placed on the inlet ports of the POCone, the instrument draws in samples from the 2 bags in sequence. It automatically removes moisture from the breath and meters the samples into the measurement cell. Light from a temperature-stabilized infrared light source passes through a mechanical chopper and then through each gas sample. The intensity of the transmitted signal is measured by a cooled infrared detector. The instrument measures absorption of breath gas by calculating the ratios of $^{13}CO_2/^{12}CO_2$ for the reference breath gas and sample breath gas. The difference between the ratios

is calculated to obtain the final measurement result, which is reported as Δ^{13} CO_2 and expressed as delta per mil (‰) or delta over baseline (DOB). Internal algorithms calculate the isotope ratios and report the result to the display screen and on an integral printer.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-run, between-run and between-day precision of the POCone was assessed by replicate measurements of standard gas samples. Testing consisted of 3 separate runs for 3 days at 3 sites. There were 10 consecutive replicate measurements performed for each of 3 levels of paired standard gas samples. Standard gas samples represented low, borderline and high results for C-urea breath test. Paired samples represented baseline and post-dose breath samples. A single outlier observation was noted at one site and data was analyzed including and excluding this point. Performance claims were met when this outlier was excluded and due to its magnitude, no difference was made to the clinical decision. Within-run precision was assessed by replicate measurements of human breath samples. Paired baseline and post-dose breath samples were collected from 5 subjects (3 positive and 2 negative) and 10 consecutive replicate measurements were performed and processed using POCone. For both studies, individual replicate results as well as mean and standard deviation were calculated. The performance claim for the POCone is a standard deviation of not more than 0.3 ‰ and the claim was met for all subjects. The POCone performed according to specifications.

b. Linearity/assay reportable range:

Paired delta over baseline (DOB) values were compared for the POCone spectrophotometer and the predicate device to determine if they were linearly related and the degree to which they were correlated. Data for all subjects gave a correlation of 0.9994, a slope of 0.9886 and an intercept of -0.0370. Both methods gave results that were very highly correlated and appeared to be linearly related to one another. Data suggested that the regression line passed through the origin with a slope very near one.

c. Traceability (controls, calibrators, or method):

Traceability between the requirements of the Software Requirements Specification (SRS), Hazard Analysis, Software Design Specification (SDS), and Validation Testing was provided in the Verification and Validation testing document. It verified that all functional and safety requirements have been tested and confirmed by the validation testing.

d. Detection limit:
The cut-off value is 2.4 Delta Over Baseline (DOB). Values below 2.4 DOB were interpreted as negative and values greater than or equal to 2.4 were interpreted as positive

e. Analytical specificity:
N/A

f. Assay cut-off:
A cut-off value histogram showing the performance of the POCone relative to the predicate showed that the POCone can successfully discriminate between negative and positive cases. The histogram used a Delta Over Baseline of 2.4 as the critical cut-off value

2. Comparison studies:

a. Method comparison with predicate device:
A multi center prospective study was conducted to compare the POCone to the predicate device. A total of 220 subjects either asymptomatic or experiencing dyspepsia, between the ages of 18 and 75 were recruited from 5 physician office labs and point of care settings. Subjects underwent standard urea breath testing with the UBT collection kit for H. pylori. Breath samples were analyzed by both the POCone and the predicate device. The percent agreement for the POCone results compared to the predicate using a cut off value of 2.4 Delta Over Baseline was as follows:
% Overall Agreement: 99.55% (97.67 %-99.98% C.I.)
% Positive Agreement: 100% (95.90%-100% C.I.)
% Negative Agreement: 99.25%(96.27%-99.96% C.I.)
There was one discrepant result. A 65 year old female with no prior history of H.pylori infection underwent breath testing according to protocol. No device malfunctions were reported. A negative result of 0.8 was reported by the predicate device and a positive result of 3.1 was reported by the POCone.
Comparison was also done of paired DOB values from the POCone and the predicate and the extent to which they were linearly related and the degree to which they were correlated. Analysis showed that both the predicate and device gave results that were highly correlated and appeared to be linearly related to one another. Data for all subjects resulted in a correlation of 0.994, a slope of 0.9886 and an intercept of -0.0370.

b. Matrix comparison:
N/A

3. Clinical studies:

a. Clinical sensitivity:

N/A

b. Clinical specificity:
N/A

c. Other clinical supportive data (when a and b are not applicable):
N/A

4. Clinical cut-off:
See assay cut off above 1(f)

5. Expected values/Reference range:
N/A

N. Instrument Name:
POCone Infrared Spectrophotometer

O. System Descriptions:
1. Modes of Operation:
Automatic
2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
Yes _X_ or No _____

Interactive software uses an operating system, which is embedded in the internal CPU
3. Sample Identification:
Patient ID can be input by key operation or ID read by barcode reader
4. Specimen Sampling and Handling:
Patient provides breath samples by blowing into breath collection bags. Two samples are provided namely the initial reference sample and after ingestion of C-urea, the post dose sample. Breath collection bags are manually placed on the inlet ports of the POCone for gas measurement analysis.
5. Assay Types:
Infrared spectrophotometric assay
6. Reaction Types:
Measurement of changes in ratio of $^{13}CO_2/^{12}CO_2$ in breath samples
7. Calibration:
The instrument self-calibrates.
8. Quality Control:
The POCone automatically performs self-diagnostic instrument checks. It is also recommended that the precision of the instrument be checked regularly, at least once a month. Additionally each laboratory should follow procedures it has established for internal quality control

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination Decision Summary:

A carry over study was conducted to assess the potential for results to be affected by widely differing $^{13}CO_2/^{12}CO_2$ ratios being carried from one sample measurement into subsequent sample measurements. 3 POCone instruments were used and samples consisted of 2 standard gases with different $^{13}CO_2/^{12}CO_2$ ratios in cylinders containing 3% CO_2 . Serial and alternate measurements were performed with both standard gases. Results demonstrated negligible carry over and inter-instrument variability.

Q. Conclusion:

The submitted material in this premarket notification is complete and supports a substantial equivalence decision.